



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,958	01/31/2005	Clarence W Andrews III	PU4870USW	6658

23347 7590 02/01/2008
GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B475
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER

LOEWE, SUN JAE Y

ART UNIT	PAPER NUMBER
----------	--------------

1626

NOTIFICATION DATE	DELIVERY MODE
-------------------	---------------

02/01/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM
ROSALIE.M.CHAMBERLAIN@GSK.COM
JULIE.D.MCFALLS@GSK.COM

Office Action Summary	Application No. 10/522,958	Applicant(s) ANDREWS ET AL.	
	Examiner Sun Jae Y. Loewe	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21, 23, 25-30, 43, 44 and 46 is/are pending in the application.
- 4a) Of the above claim(s) 25-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 8, 15, 16, 18, 19, 21 and 23 is/are rejected.
- 7) ☒ Claim(s) 2-7, 9-14, 17, 20, 43, 44 and 46 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11-30-2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-21, 23, 25-30, 43, 44 and 46 are pending in the instant application. Claims 22, 24, 31 and 32 were cancelled by amendment filed on August 15, 2007. Claim 45 was cancelled by preliminary amendment filed on April 26, 2006. Claims 33-42 were cancelled on January 31, 2005.

Response to Arguments

2. Applicant's arguments have been fully considered.
3. The 35 USC 102 rejection (Section 9, office action dated August 27, 2007) is withdrawn. See new ground of rejection under 35 USC 103 (below, Section 12).
4. The claim objections (Section 5, office action dated August 27, 2007) are maintained. See response to arguments below, Sections 7 and 8.
5. The 35 USC 112 1st paragraph rejections (Sections 6 and 7, office action dated August 27, 2007) are maintained. See response to arguments below, Section 10.
6. A new ground of objection is set forth in Section 9.

Election/Restrictions

7. Applicant's election of species was acknowledged in the action dated August 27, 2007). It was stated therein that the guidelines of MPEP § 803.02 were followed for search and examination. See excerpts of MPEP § 803.02:

“In applications

containing a Markush-type claim that encompasses at least two independent or distinct inventions, the examiner may require a provisional election of a single species prior to examination on the merits.

examiner should set forth a requirement for election of a single disclosed species in a Markush-type claim using form paragraph 8.01 when claims limited to species are present or using form paragraph 8.02 when no species claims are present.

Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability.

If the Markush-type claim is not allowable **, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. ”

The Markush-type claim was not allowable, therefore the provisional election was given effect and non-elected species were withdrawn from further consideration.

Applicant's attention is directed to Form Paragraph 8.01 referenced above:

“ ¶ 8.01 *Election of Species; Species Claim(s) Present*

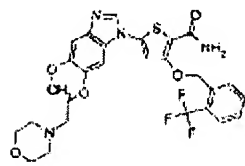
Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141 ”

In order to be entitled for consideration of non-elected species, Applicant must overcome all outstanding grounds of rejection of the generic Markush-type claims.

Notwithstanding the withdrawal of the 35 USC 102 rejection (see section 3, above), the Markush type claims remain rejected under 35 USC 112.

Claim Objections

8. Pursuant MPEP § 803.02, the elected subject matter is the compound of



(see response dated August 15, 2007). The non-elected subject matter (currently withdrawn) is: species within the scope of claims 1-21, 23, 43, 44 and 46 that is not the elected species. Consequently, claims 1-21, 23, 43, 44 and 46 remain objected to for containing non-elected subject matter.

Information Disclosure Statement

9. The information disclosure statement (IDS) submitted on November 30, 2007 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is submitted herewith.

10. Claim 20 objected to because of the following informality: the claim is not written in proper Markush form. The following corrections are suggested: add the term "and" between the last two compounds listed; replace " and pharmaceutically acceptable salts thereof," with "or a pharmaceutically acceptable salt thereof."

Claim Rejections - 35 USC § 112

11. Response to Applicant's arguments addressed below.

(Written Description)

- a) "Applicants respectfully submit that the outstanding rejection improperly fails to account for the level of skill in the art at the time of filing. . . .
the rejection fails to apply this high level of skill to the analysis. Accordingly, the Examiner's burden has not been met and the rejection should be withdrawn on these grounds. "

The level of ordinary skill is addressed on p. 7 the office action dated August 27, 2007:

“In the absence of a correlation between structure and function (with scope commensurate with that instantly claimed), it is not possible to determine which structural modifications will lead to compounds that are inhibitors of polo-like kinase.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-19, 21, 23 and 43; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.”

One of ordinary skill in the art is aware that structural/chemical modifications, *in the absence of evidence to the contrary*, results in changes to the ability of a compound to modulate an enzyme/receptor. This determination was considered in the analysis, see excerpts above.

- b) “Cheung article referenced by the Examiner was published approximately 5 years after the filing date of the instant application and thus has no bearing on the analysis because written description must be analyzed as of the filing date of the application.”

The following citation by the Applicant is noted:

“should include a determination of the field of the invention and the level of skill and knowledge in the art. Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of the disclosure necessary to satisfy written description.” *Id.*

The reference of M. Cheung et al. establishes the level of knowledge/ordinary skill in the art at a time that is later than the filing date of the application. It is asserted that the level of knowledge/ordinary skill in the art at the time of filing is, at best, equivalent to the level of ordinary skill at the time of the reference. Thus, the reference is relevant in establishing the “upper boundary” for the level of ordinary skill/knowledge at the time the instant application was filed.

- c) “a generic formula is normally adequate in chemical cases to meet written description for the claimed genus, because one skilled in the art can visualize many of the species that the claims encompass.
...
In chemical cases, including the instant claims, a generic structural definition is sufficient to meet the written description guidelines.”

Applicant is referred to pg. 5 of the previous office action. See excerpts below:

“ The MPEP states that for a generic claim the genus can be adequately described if the

disclosure presents a sufficient number of representative species that encompass the genus.

.....

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure."

It is maintained that a sufficient number of representative species was not disclosed, by any (or the additive combination) of the methods denoted above in a)-c), so as to adequately describe the genus. This determination was the basis of Section 6.II. of the office action dated August 27, 2007.

- d) "Applicants have provided a structural formula, definitions of variables and term, guidance and direction toward particular embodiments and over 150 individual species."

It is maintained that support for the claimed genus must be in form of representative species. It is also maintained that the definition of variables and embodiments (ie. subgenuses) do not constitute "representative species" (ie. see office action dated August 27, 2007; section 6.II). Lastly, the "150 individual species" noted by Applicant does not comprise "a sufficient number of representative species" for the reasons provided in Section 6.II. of the previous office action. For example, the totality of the "150 individual species" provides support for compounds wherein R6=phenyl, which are not representative of compounds wherein R6=Het. Of the "150 individual species", there is not a single species for which R6=Het. It is further noted that the term "Het" is in and of itself drawn to a large genus with substantial structural variability (see definition quoted on pg. 16 of the remarks filed on November 30, 2007

(Enablement)

- e) "Claims 1-19, 21, 23 and 43 currently stand rejected under 35 U.S.C. §112, first paragraph, the Office Action stating that the specification fails to enable those compounds identified in the prior rejection as lacking adequate written description. ... That an element of a claim lacks written description does not necessarily lead to the conclusion that it is also not enabled. MPEP 2164."

The following was set forth in the office action dated August 27, 2007:

The breadth of the claims
"Compounds not supported by the disclosure (see above section 6.I and 6.II.).". The reference to Section 6.I. and 6.II. was provided to identify the scope/breadth of the subject matter discussed in the analysis of the Wands factors. Thus, the analysis used to evaluate of enablement (Section 7, office action dated August 27, 2007) was performed independently from the analysis used to

evaluate written description (section 6, office action dated August 27, 2007).

f)

“Based upon the variety of the exemplified compounds

represented and the biological data provided there is no reason one skilled in the art not provided objective evidence to establish the contrary. The Cheung publication does not provide the requisite evidence because the publication occurred in July 2007, nearly 5 years after the application priority date. The Examiner is required to consider enablement at the time the invention was made, not in light of publications made 5 years later.”

The reference of M. Cheung was quoted to provide evidence of the low level of predictability in the art of inhibiting polo-like kinase with compounds of the instant genus. Applicant is referred to MPEP § 2164.05 (a) – excerpts below:

“While a later dated

publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. *Gould v. Quigg*, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987).

In general, the examiner should not use post-filing date references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application. *In re Hogan*, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977). If individuals of skill in the art state that a particular invention is not possible years after the filing date, that would be evidence that the disclosed invention was not possible at the time of filing and should be considered. In *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513-14 (Fed. Cir. 1993) an article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms. Claims not directed to the specific virus and the specific animal were held nonenabled.”

g)

“The Examiner has argued that without correlation between activity and specific structural elements of Q¹ and Q², one skilled in the art would be unable to “predict” what structural modifications within other compounds, would lead to active compounds. This is not the standard for enablement.”

MPEP § 2164.03 states:

“The scope of the required enablement varies

inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soil*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaack*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. ”

The reference of M. Cheung was used to establish unpredictability. The statements made in Section 7 of the office action dated August 27, 2007 were provided to ascertain this low level of predictability.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

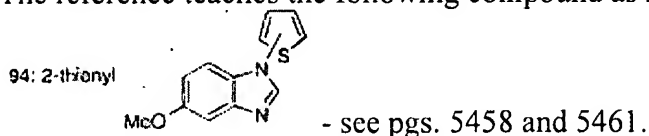
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
12. Claims 1, 8, 15, 16, 17, 18, 19, 21 and 23 rejected under 35 U.S.C. 103(a) as being obvious over Palmer et al.

Determination of the scope and contents of prior art.

The reference teaches the following compound as ATP-site inhibitor



Ascertaining the differences between prior art and instant claims.

The prior art compound makes obvious the following non-elected species: compounds with the structural limitations of $R^1=R^5=H$; $Q^1 = -(R^2)_a-(Y^1)_b-(R^3)_c-R^4$ with $a=1$, $R^2=alkylene$, $b=c=0$; $R^3=H$; $n=1$; $Q^2 = -(R^2)_{aa}-(Y^2)_{bb}-(R^3)_{cc}-R^4$ with $aa=0$, $bb=1$, $Y^2=-O-$, $(cc=1, R^2=alkylene, R^4=H)$ or $(cc=0, R^4=alkyl)$.

The following modification to the prior art compound results in the non-elected species shown above: hydrogen substitution at the 4-position of the thiophene ring is replaced by alkyl. Thus, the prior art compound is a homolog of the non-elected species.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

To those skilled in chemical art, one homologue is not an advance over another member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

One of ordinary skill would be motivated, from the disclosure of Palmer et al., to make the modification required to arrive at the instant invention with reasonable expectation of success for obtaining a compound with the same activity. The motivation to make these changes would be to make additional compounds for the quoted purpose.

Thus, the instant claims are *prima facie* obvious over the teaching of the prior art.

Conclusion

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SL
1-25-2008

REBECCA ANDERSON
PRIMARY EXAMINER

Rebecca Anderson
Primary Examiner
Art Unit 1626

